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☐	L29	L28 and TADG-14	8
☐	L28	L27 and (serine)adj(protease)	2315
☐	L27	435/326,252.8,410,252.33,69.1,536/23.2.ccls.	31339
☐	L26	(shigemasa)adj(kazushi)	7
☐	L25	L24 and TADG-14	4
☐	L24	(beard)adj(john)	78
☐	L23	L22 and 1343	9
☐	L22	L21 and TADG-14	12
☐	L21	(underwood)adj(lowell)adj(j)	20
☐	L20	L17 and (1343)	9
☐	L19	L17 and (1343)adj(basepair)	0
☐	L18	L17 and (1343)adj(bp)	0
☐	L17	L16 and nucleic	26
☐	L16	L15 and variant	26
☐	L15	L14 and TADG-14	28
☐	L14	(OBrien)adj(timothy)adj(j)	91
☐	L13	L12 and (305)adj(amino)adj(acid)	1
☐	L12	L11 and nucleic	147
☐	L11	(human)adj(neuropsin)	148
☐	L10	L5 and (human)adj(neuropsin)	7
☐	L9	L7 and (SEQ)adj(ID)adj(NO)adj(75)	1
☐	L8	L7 and (SEQ)adj(ID)adj(NO.75)	0
☐	L7	L5 and TADG-14	13
☐	L6	L5 and (TADG-14)adj(variant)	1
☐	L5	(extracellular)adj(serine)adj(protease)	129
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NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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=> s serine protease
L1 64008 SERINE PROTEASE

=> s l1 and human neuropsin
L2 28 L1 AND HUMAN NEUROPSIN

=> dup remove l2
PROCESSING COMPLETED FOR L2
L3 16 DUP REMOVE L2 (12 DUPLICATES REMOVED)

=> d l3 1-16 cbib abs

L3 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
2006:622020 Document No. 145:78740 Cloning and sequence of human extracellular **serine protease** TADG-14 and use in cancer diagnosis. Underwood, Lowell J.; O'Brien, Timothy J. (The University of Arkansas for Medical Sciences, USA). U.S. US 7067250 B1 20060627, 37 pp., Cont.-in-part of U.S. Ser. No. 915,659. (English). CODEN: USXXAM. APPLICATION: US 1998-137944 19980821. PRIORITY: US 1997-915659 19970821.

AB The present invention relates to a novel extracellular **serine protease** termed tumor antigen derived gene-14 (TADG-14) which is overexpressed in ovarian, breast and colon carcinoma samples. The present invention provides a DNA encoding a TADG-14 protein selected from the group consisting of: (a) isolated DNA which encodes a TADG-14 protein; (b) isolated DNA which hybridizes to isolated DNA of (a) above and which encodes a TADG-14 protein; and (c) isolated DNA differing from the isolated DNAs of (a) and (b) above in codon sequence due to the degeneracy of the genetic code, and which encodes a TADG-14 protein. Also provided is a vector capable of expressing the DNA of the present invention adapted for expression in a recombinant cell and regulatory elements necessary for expression of the DNA in the cell. The present invention discloses a screening system to identify proteases overexpressed in carcinoma by examining PCR products amplified from early-stage tumors, metastatic tumor,

and normal ovarian epithelium.

L3 ANSWER 2 OF 16 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

2006:273422 The Genuine Article (R) Number: 021MT. Human kallikrein 8 protein is a favorable prognostic marker in ovarian cancer. Borgono C A; Kishi T; Scorilas A; Harbeck N; Dorn J; Schmalfeldt B; Schmitt M; Diamandis E P (Reprint). Univ Toronto, Mt Sinai Hosp, Dept Pathol & Lab Med, 600 Univ Ave, Toronto, ON M5G 1X5, Canada (Reprint); Univ Toronto, Mt Sinai Hosp, Dept Pathol & Lab Med, Toronto, ON M5G 1X5, Canada; Univ Toronto, Dept Lab Med & Pathobiol, Toronto, ON M5G 1X5, Canada; Univ Athens, Fac Biol, Dept Biochem & Mol Biol, Athens, Greece; Tech Univ Munich, Dept Obstet & Gynecol, Clin Res Unit, D-8000 Munich, Germany. ediamandis@mtsinai.on.ca. CLINICAL CANCER RESEARCH (1 MAR 2006) Vol. 12, No. 5, pp. 1487-1493. ISSN: 1078-0432. Publisher: AMER ASSOC CANCER RESEARCH, 615 CHESTNUT ST, 17TH FLOOR, PHILADELPHIA, PA 19106-4404 USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Human kallikrein 8 (hK8/neuropsin/ovasin; encoded by KLK8) is a steroid hormone-regulated secreted **serine protease** differentially expressed in ovarian carcinoma. KLK8 mRNA levels are associated with a favorable patient prognosis and hK8 protein levels are elevated in the sera of 62% ovarian cancer patients, suggesting that KLK8/hK8 is a prospective biomarker. Given the above, the aim of the present study was to determine if tissue hK8 bears any prognostic significance in ovarian cancer. Using a newly developed ELISA, hK8 was quantified in 136 ovarian tumor extracts and correlated with clinicopathologic variables and outcome [progression-free survival (PFS); overall survival (OS)] over a median follow-up period of 42 months. hK8 levels in ovarian tumor cytosols ranged from 0 to 478 ng/mg total protein, with a median of 30 ng/mg. An optimal cutoff value of 25.8 ng/mg total protein (74th percentile) was selected based on the ability of hK8 values to predict the PFS of the study population and to categorize tumors as hK8 positive or negative. Women with h K8-positive tumors most often had lower-grade tumors (G1), no residual tumor after surgery, and optimal debulking success ($P < 0.05$). Univariate and multivariate analyses revealed that patients with hK8-positive tumors had a significantly longer PFS and OS than hK8-negative patients ($P < 0.05$). Kaplan-Meier survival curves further confirmed a reduced risk of relapse and death in women with hK8-positive tumors ($P = 0.001$ and $P = 0.014$, respectively). These results indicate that hK8 is an independent marker of favorable prognosis in ovarian cancer.

L3 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN

2004:371153 Document No. 140:371494 Binary prediction tree modeling with many predictors and its uses in clinical and genomic applications. Nevins, Joseph R.; West, Mike; Huang, Andrew T. (Duke University, USA). PCT Int. Appl. WO 2004038376 A2 20040506, 886 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US33946 20031024. PRIORITY: US 2002-420729P 20021024; US 2002-421062P 20021025; US 2002-421102P 20021025; US 2002-424715P 20021108; US 2002-424718P 20021108; US 2002-424701P 20021108; US 2002-425256P 20021112; US 2003-448462P 20030221; US 2003-448461P 20030221; US 2003-457877P 20030327; US 2003-458373P 20030331.

AB The statistical anal. described and claimed is a predictive statistical tree model that overcomes several problems observed in prior statistical models and regression analyses, while ensuring greater accuracy and predictive capabilities. Although the claimed use of the predictive statistical tree model described herein is directed to the prediction of a

disease in individuals, the claimed model can be used for a variety of applications including the prediction of disease states, susceptibility of disease states or any other biol. state of interest, as well as other applicable non-biol. states of interest. This model first screens genes to reduce noise, applies kmeans correlation-based clustering targeting a large number of clusters, and then uses singular value decompns. (SVD) to extract the single dominant factor (principal component) from each cluster. This generates a statistically significant number of cluster-derived singular factors, that are referred to as metagenes, that characterize multiple patterns of expression of the genes across samples. The strategy aims to extract multiple such patterns while reducing dimension and smoothing out gene-specific noise through the aggregation within clusters. Formal predictive anal. then uses these metagenes in a Bayesian classification tree anal. This generates multiple recursive partitions of the sample into subgroups (the 'leaves' of the classification tree), and assocs. Bayesian predictive probabilities of outcomes with each subgroup. Overall predictions for an individual sample are then generated by averaging predictions, with appropriate wts., across many such tree models. The model includes the use of iterative out-of-sample, cross-validation predictions leaving each sample out of the data set one at a time, refitting the model from the remaining samples and using it to predict the hold-out case. This rigorously tests the predictive value of a model and mirrors the real-world prognostic context where prediction of new cases as they arise is the major goal.

L3 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN

2004:371064 Document No. 140:373461 Evaluation of breast cancer states and outcomes using gene expression profiles. West, Mike; Nevins, Joseph R.; Huang, Andrew (Synpac, Inc., USA; Duke University). PCT Int. Appl. WO 2004037996 A2 20040506, 799 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US33656 20031024. PRIORITY: US 2002-420729P 20021024; US 2002-421102P 20021025; US 2002-421062P 20021025; US 2002-424701P 20021108; US 2002-424718P 20021108; US 2002-424715P 20021108; US 2002-425256P 20021112; US 2002-291878 20021112; US 2002-291886 20021112; WO 2002-US38222 20021112; WO 2002-US38216 20021112; US 2003-448462P 20030221; US 2003-448461P 20030221; US 2003-457877P 20030327; US 2003-458373P 20030331.

AB The present invention relates generally to a method for evaluating and/or predicting breast cancer states and outcomes by measuring gene and metagene expression levels and integrating such data with clin. risk factors. Genes and metagenes whose expressions are correlated with a particular breast cancer risk factor or phenotype are provided using binary prediction tree modeling. The invention provides 175 genes associated with metagene predictors of lymph node metastasis, 216 genes associated with metagene predictors of breast cancer recurrence, and 496 metagenes related to breast cancer study. Methods of using the subject genes and metagenes in diagnosis and treatment methods, as well as drug screening methods, etc are also provided. In addition, reagents, media and kits that find use in practicing the subject methods are also provided.

L3 ANSWER 5 OF 16 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

2005:42873 Document No.: PREV200500046525. Recent origin of a hominoid-specific splice form of neuropsin, a gene involved in learning and memory. Li, Yi; Qian, Ya-ping; Yu, Xiao-jing; Wang, Yin-qiu; Dong, Ding-gui; Sun, Wei; Ma, Run-mei; Su, Bing [Reprint Author]. Kunming Inst ZoolKey Lab Cellular and Mol Evolut, Chinese Acad Sci, Kunming, Yunnan, China. sub@mail.kiz.ac.cn. Molecular Biology and Evolution, (November 2004) Vol. 21, No. 11, pp. 2111-2115. print.

CODEN: MBEVEO. ISSN: 0737-4038. Language: English.

AB Neuropsin is a secreted-type **serine protease** involved in learning and memory. The type II splice form of neuropsin is abundantly expressed in the human brain but not in the mouse brain. We sequenced the type II-spliced region of neuropsin gene in humans and representative nonhuman primate species. Our comparative sequence analysis showed that only the hominoid species (humans and apes) have the intact open reading frame of the type II splice form, indicating that the type II neuropsin originated recently in the primate lineage about 18 MYA. Expression analysis using RT-PCR detected abundant expression of the type II form in the frontal lobe of the adult human brain, but no expression was detected in the brains of lesser apes and Old World monkeys, indicating that the type II form of neuropsin only became functional in recent time, and it might contribute to the progressive change of cognitive abilities during primate evolution.

L3 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN

2004:927860 Document No. 142:293429 Neuropsin, human tissue kallikrein 8. Kishi, Tadaaki; Diamandis, Eleftherios P. (Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, ON, M5G 1X5, Can.). Handbook of Proteolytic Enzymes (2nd Edition), Volume 2, 1591-1593. Editor(s): Barrett, Alan J.; Rawlings, Neil D.; Woessner, J. Fred. Elsevier: London, UK. ISBN: 0-12-079610-4 (English) 2004. CODEN: 69GAQF.

AB A review. A novel **serine protease** that was predicted to have trypsin-like structure was cloned from a mouse hippocampus cDNA library and named neuropsin. Identified as a gene highly expressed in ovarian carcinoma, **human neuropsin** is also described as ovasin or tumor-associated differentially expressed gene 14 (TADG-14). Recently, the **human neuropsin** gene was mapped to chromosome 19q13.4 and identified as a member of the human kallikrein gene family. An international working party proposed to describe **human neuropsin** gene and protein as KLK8 and hK8, resp. The activity, specificity, structural chemical, preparation, biol. aspects, and distinguishing features of neuropsin or human kallikrein 8 are briefly discussed.

L3 ANSWER 7 OF 16 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

2005:30491 Document No.: PREV200500032102. **Serine proteases** regulating synaptic plasticity. Shiosaka, Sadao [Reprint Author]. Div Struct Cell Biol, Nara Inst Sci and Technol, 8916-5 Takayama, Nara, 6300192, Japan. sshiosak@bs.naist.jp. Anatomical Science International, (September 2004) Vol. 79, No. 3, pp. 137-144. print. ISSN: 1447-6959 (ISSN print). Language: English.

AB A number of molecules have been postulated to be involved in long-term potentiation, an experimental model for learning and short-term memory. Although the molecular mechanisms of the long-term potentiation have been considerably well understood, it is not yet known why and how real memory can last very long with outstanding stability. A mechanical change of synaptic morphology at acquisition, consolidation and retention of memory is hypothesized to explain long-lasting memory. Changes in the synaptic morphology may be due, at least in part, to local extracellular proteolysis of cell adhesion and extracellular matrix molecules. Some extracellular **serine proteases** of the Clan PA family may modulate synaptic adhesion and associate with longterm potentiation and learning behavior. In the present review, candidate proteases that are involved in the hippocampal memory are overviewed.

L3 ANSWER 8 OF 16 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

2003:709262 The Genuine Article (R) Number: 707KP. Characterization of the enzymatic activity of human kallikrein 6: autoactivation, substrate specificity, and regulation by inhibitors. Magklara A; Mellati A A; Wasney G A; Little S P; Sotiropoulou G; Becker G W; Diamandis E P (Reprint). Mt Sinai Hosp, Dept Pathol & Lab Med, 600 Univ Ave, Toronto, ON M5G 1X5, Canada (Reprint); Mt Sinai Hosp, Dept Pathol & Lab Med, Toronto,

ON M5G 1X5, Canada; Univ Toronto, Dept Lab Med & Pathobiol, Toronto, ON M5G 1L5, Canada; Lilly Res Labs, Cent Nervous Syst Res, Indianapolis, IN 46285 USA; Univ Patras, Dept Pharm, Patras, Greece; Roche Diagnost Corp, Indianapolis, IN USA. BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS (8 AUG 2003) Vol. 307, No. 4, pp. 948-955. ISSN: 0006-291X. Publisher: ACADEMIC PRESS INC ELSEVIER SCIENCE, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Human kallikrein 6 (hK6) is a trypsin-like **serine protease**, member of the human kallikrein gene family. Studies suggested a potential involvement of hK6 in the development and progression of Alzheimer's disease. The serum levels of hK6 might be used as a biomarker for ovarian cancer. To gain insights into the physiological role of this enzyme, we sought to determine its substrate specificity and its interactions with various inhibitors. We produced the proform of hK6 and showed that this enzyme was able to autoactivate, as well as proteolyse itself, leading to inactivation. Kinetic studies indicated that hK6 cleaved with much higher efficiency after Arg than Lys and with a preference for Ser or Pro in the P2 position. The efficient degradation of fibrinogen and collagen types I and IV by hK6 indicated that this kallikrein might play a role in tissue remodeling and/or tumor invasion and metastasis. We also demonstrated proteolysis of amyloid precursor protein by hK6 and determined the cleavage sites at the N-terminal end of the protein. Inhibition of hK6 was achieved via binding to different serpins, among which antithrombin III was the most efficient.

L3 ANSWER 9 OF 16 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

2003:72499 The Genuine Article (R) Number: 631YK. Human kallikrein 8: Immunoassay development and identification in tissue extracts and biological fluids. Kishi T; Grass L; Soosaipillai A; Shimizu-Okabe C; Diamandis E P (Reprint). Mt Sinai Hosp, Dept Pathol & Lab Med, 600 Univ Ave, Toronto, ON M5G 1X5, Canada (Reprint); Mt Sinai Hosp, Dept Pathol & Lab Med, Toronto, ON M5G 1X5, Canada; Univ Toronto, Dept Lab Med & Pathobiol, Toronto, ON M5G 1L5, Canada; Hamamatsu Univ, Sch Med, Dept Physiol, Hamamatsu, Shizuoka 4313192, Japan. CLINICAL CHEMISTRY (JAN 2003) Vol. 49, No. 1, pp. 87-96. ISSN: 0009-9147. Publisher: AMER ASSOC CLINICAL CHEMISTRY, 2101 L STREET NW, SUITE 202, WASHINGTON, DC 20037-1526 USA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Background: The **serine protease** human kallikrein 8 (hK8; neuropsin), a new member of the human kallikrein family, was predicted to be secreted; thus, it is expected to be present in biological fluids. The aim of this study was to develop a sensitive and specific immunoassay for hK8 (hK8-ELISA) and establish the distribution of hK8 in tissue extracts and biological fluids.

Methods: Recombinant hK8 was produced in a baculovirus expression system and purified with a three-step chromatographic procedure. Purified hK8 was injected into mice and rabbits for antibody generation. A highly specific and sensitive sandwich-type immunoassay (ELISA) was developed using the rabbit and mouse antisera to hK8. The hK8-ELISA was then used to study the distribution of hK8 in various biological fluids and tissue extracts.

Results: The dynamic range of the hK8-ELISA was 0.2 (detection limit) to 20 mug/L, and imprecision (CV) was <10% within this range. This hK8-ELISA was specific for hK8 and had no detectable cross-reactivity with other members of the human kallikrein family. With this assay, hK8 was detected in tissue extracts of esophagus (highest concentrations), skin, testis, tonsil, kidney, breast, and salivary gland and in the biological fluids breast milk (highest concentrations), amniotic fluid, seminal plasma, and serum. Furthermore, in some cancer cell lines, the concentration of hK8 was regulated by steroid hormones.

Conclusions: We report for the first time production of recombinant hK8 protein, generation of antibodies, and development of a highly

sensitive and specific immunoassay for quantification of hK8 in tissue extracts and biological fluids. This assay can be used to explore the potential of hK8 as a marker of cancer or other conditions. (C) 2003 American Association for Clinical Chemistry.

L3 ANSWER 10 OF 16 MEDLINE on STN DUPLICATE 1
2002441103. PubMed ID: 12147714. Epidermal expression of **serine protease**, neuropsin (KLK8) in normal and pathological skin samples. Kuwae K; Matsumoto-Miyai K; Yoshida S; Sadayama T; Yoshikawa K; Hosokawa K; Shiosaka S. (Department of Plastic Surgery, Osaka University Medical School, Osaka, Japan.) Molecular pathology : MP, (2002 Aug) Vol. 55, No. 4, pp. 235-41. Journal code: 9706282. ISSN: 1366-8714. Pub. country: England: United Kingdom. Language: English.

AB AIMS: The expression of **human neuropsin** (KLK8) mRNA in normal and pathological skin samples was analysed and the results compared with those for tissue plasminogen activator (tPA) mRNA. METHODS: Northern blot and in situ hybridisation analyses of KLK8 mRNA in normal and lesional skin of patients with cutaneous diseases were performed. RESULTS: A weak signal for KLK8 mRNA and no signal for tPA mRNA was seen in normal skin on northern blot analysis. Weak signals for KLK8 were localised to the superficial cells beneath the cornified layer in normal skin on in situ hybridisation. Psoriasis vulgaris, seborrheic keratosis, lichen planus, and squamous cell carcinoma skin samples, which show severe hyperkeratosis, displayed a high density of KLK8 mRNA on northern and in situ hybridisation analyses. The signals were localised in granular and spinous layers of lesional skin in all hyperkeratic samples, including the area surrounding the horn pearls of squamous cell carcinoma. To examine the relation between mRNA expression and terminal differentiation, the expression of KLK8 mRNA was analysed in cell cultures. When keratinisation proceeded in high calcium medium, a correlative increase in the expression of KLK8 mRNA was observed. CONCLUSION: The results are consistent with a role for this protease in the terminal differentiation of keratinocytes.

L3 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
2001:123822 Document No. 134:176271 Human brain-related **serine protease** neuropsin, expressed by alternative splicing. Tsuruoka, Nobuo; Yamashiro, Kyoko; Mitsui, Shinichi; Yamaguchi, Nozomi (Suntory, Ltd., Japan). Jpn. Kokai Tokkyo Koho JP 2001046065 A 20010220, 24 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1999-220522 19990803.

AB **Serine protease** neuropsin, expressed as splice variants in human brain, cDNA clones, antisense DNA, recombinant expression, antibodies, and use in drug screening, are disclosed. We have cloned cDNAs encoding two isoforms of a human novel **serine protease.** They encoded sequences of 260 and 305 amino acids, and both showed significant homol. to mouse neuropsin. Mouse neuropsin has been reported to be involved in hippocampal plasticity, therefore we designated the proteins as type 1 and type 2 neuropsin, resp. The amino acid sequences of the two types of **human neuropsin** were identical, except that type 2 carried an insert of 45 amino acids at the C-terminus of the leader sequence. The essential three amino acids in the active site triad, His, Asp, and Ser, and the single putative N-glycosylation site were conserved in human and mouse neuropsin. Sequence anal. of the 946 bp genomic DNA spanning the region encoding the insertion sequence revealed that two isoforms were generated in human brain by alternative splicing. However, the mouse genomic sequence did not conserve the 3' acceptor consensus sequence at the corresponding position, suggesting that type 2 neuropsin was a species-specific splice variant. When the open reading frames of **human neuropsin** were expressed in Sf9 insect cells, both types of neuropsin were detected in the conditioned media by western blot anal. using anti-**human neuropsin** serum. Northern blot hybridization and reverse transcription-polymerase chain reaction showed predominant expression of type 1 neuropsin in pancreas. Type 2 neuropsin was preferentially expressed in human adult brain and hippocampus,

although both types were expressed in fetal brain and placenta in comparable amts. Dot blot hybridization showed that neuropsin was expressed in various regions of adult brain, including the hippocampus and cerebral cortex, and also in various fetal tissues. These results suggest that human type 2 neuropsin may be important to the adult brain plasticity, although both types may be necessary for the development of the nervous system.

L3 ANSWER 12 OF 16 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

2001:61487 The Genuine Article (R) Number: 390DP. Molecular cloning of the human kallikrein 15 gene (KLK15) - Up-regulation in prostate cancer. Yousef G M; Scorilas A; Jung K; Ashworth L K; Diamandis E P (Reprint). Mt Sinai Hosp, Dept Pathol & Lab Med, 600 Univ Ave, Toronto, ON M5G 1X5, Canada (Reprint); Mt Sinai Hosp, Dept Pathol & Lab Med, Toronto, ON M5G 1X5, Canada; Univ Toronto, Dept Lab Med & Pathobiol, Toronto, ON M5G 1L5, Canada; Humboldt Univ, Univ Hosp Berlin, Charite, Dept Urol, D-10048 Berlin, Germany; Univ Calif Lawrence Livermore Natl Lab, Biol & Biotechnol Program, Livermore, CA 94551 USA. JOURNAL OF BIOLOGICAL CHEMISTRY (5 JAN 2001) Vol. 276, No. 1, pp. 53-61. ISSN: 0021-9258. Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3996 USA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Kallikreins are a subgroup of **serine proteases** with diverse physiological functions. Growing evidence suggests that many kallikreins are implicated in carcinogenesis. By using molecular cloning techniques, we identified a new human kallikrein gene, tentatively named KLK15 (for Kallikrein 15 gene). This new gene maps to chromosome 19q13.4 and is located between the KLK1 and KLK3 genes. KLK15 is formed of five coding exons and four introns, and shows structural similarity to other kallikreins and kallikrein-like genes. KLK15 has three alternatively spliced forms and is primarily expressed in the thyroid gland and to a lower extent in the prostate, salivary, and adrenal glands and in the colon testis and kidney. Our preliminary results indicate that the expression of KLK15 is up-regulated by steroid hormones in the LNCaP prostate cancer cell line. The KLK15 gene is also up-regulated, at the mRNA level, in prostate cancer in comparison to normal prostatic tissue. KLK15 up-regulation was found to be associated with more aggressive forms of prostate cancer. This newly discovered gene has the potential of being used as a diagnostic and/or prognostic marker for prostate cancer.

L3 ANSWER 13 OF 16 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

2000:347510 The Genuine Article (R) Number: 308DP. Identification and characterization of KLK-L4, a new kallikrein-like gene that appears to be down-regulated in breast cancer tissues. Yousef G M; Chang A; Diamandis E P (Reprint). Mt Sinai Hosp, Dept Pathol & Lab Med, 600 Univ Ave, Toronto, ON M5G 1X5, Canada (Reprint); Mt Sinai Hosp, Dept Pathol & Lab Med, Toronto, ON M5G 1X5, Canada; Univ Toronto, Dept Lab Med & Pathobiol, Toronto, ON M5G 1X5, Canada. JOURNAL OF BIOLOGICAL CHEMISTRY (21 APR 2000) Vol. 275, No. 16, pp. 11891-11898. ISSN: 0021-9258. Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Kallikreins are a subgroup of **serine proteases** and these proteolytic enzymes have diverse physiological functions in many tissues. Growing evidence suggests that many kallikreins are implicated in carcinogenesis. In rodents, kallikreins constitute a large multigene family, but in humans, only three genes were identified. By using the positional candidate gene approach, we were able to identify a new kallikrein-like gene, tentatively named KLK-L4 (for kallikrein-like gene 4), This new gene maps to chromosome 19q13.3-q13.4, is formed of five coding exons and four introns, and shows structural similarity to other kallikreins and kallikrein-like genes. KLK-L4 is expressed in a variety of tissues including prostate, salivary gland, breast, and testis, Our

preliminary results show that KLK-L4 is down-regulated, at the mRNA level, in breast cancer tissues and breast cancer cell lines. Its expression is regulated by steroid hormones in the breast cancer cell line BT-474. This gene may be involved in the pathogenesis and/or progression of breast cancer and may find applicability as a novel cancer biomarker.

L3 ANSWER 14 OF 16 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

2000:852124 The Genuine Article (R) Number: 371GB. KLK12 is a novel **serine protease** and a new member of the human kallikrein gene family - Differential expression in breast cancer. Yousef G M; Magklara A; Diamandis E P (Reprint). Mt Sinai Hosp, Dept Pathol & Lab Med, 600 Univ Ave, Toronto, ON M5G 1X5, Canada (Reprint); Mt Sinai Hosp, Dept Pathol & Lab Med, Toronto, ON M5G 1X5, Canada; Univ Toronto, Dept Lab Med & Pathobiol, Toronto, ON M5G 1L5, Canada. GENOMICS (1 NOV 2000) Vol. 69, No. 3, pp. 331-341. ISSN: 0888-7543. Publisher: ACADEMIC PRESS INC, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Kallikreins are a subgroup of **serine proteases** that are involved in the posttranslational processing of polypeptide precursors, Growing evidence suggests that many kallikreins are implicated in carcinogenesis. In rodents, kallikreins are encoded by a large multigene family, but in humans, only three genes have been identified, By using the positional candidate approach, we were able to identify a new kallikrein-like gene, tentatively named KLK12 (for kallikrein gene 12). This new gene maps to chromosome 19q13.3-q13.4, is formed of five coding exons, and shows structural similarity to **serine proteases** and other known kallikreins, KLK12 is expressed in a variety of tissues including salivary gland, stomach, uterus, lung, thymus, prostate, colon, brain, breast, thyroid, and trachea, We identified three splicing forms of KLK12 that are expressed in many tissues. Our preliminary results indicate that the expression of KLK12 is downregulated at the mRNA level in breast cancer tissues and is up-regulated by steroid hormones in breast and prostate cancer cell lines, This gene may be involved in the pathogenesis and/or progression of certain cancer types and may find applicability as a novel cancer biomarker, (C) 2000 Academic Press.

L3 ANSWER 15 OF 16 MEDLINE on STN DUPLICATE 2

1999203457. PubMed ID: 10102990. A novel form of **human neuropsin**, a brain-related **serine protease**, is generated by alternative splicing and is expressed preferentially in human adult brain. Mitsui S; Tsuruoka N; Yamashiro K; Nakazato H; Yamaguchi N. (Department of Cell Biology, Institute for Neurological Diseases and Geriatrics, Kawaramachi Hirokaji, Japan.) European journal of biochemistry / FEBS, (1999 Mar) Vol. 260, No. 3, pp. 627-34. Journal code: 0107600. ISSN: 0014-2956. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB We have cloned cDNAs encoding two isoforms of a human novel **serine protease.** They encoded sequences of 260 and 305 amino acids, and both showed significant homology to mouse neuropsin. Mouse neuropsin has been reported to be involved in hippocampal plasticity, therefore we designated the proteins as type 1 and type 2 neuropsin, respectively. The amino acid sequences of the two types of **human neuropsin** were identical, except that type 2 carried an insert of 45 amino acids at the C-terminus of the leader sequence. The essential three amino acids in the active site triad, His, Asp, and Ser, and the single putative N-glycosylation site were conserved in human and mouse neuropsin. Sequence analysis of the 946 bp genomic DNA spanning the region encoding the insertion sequence revealed that two isoforms were generated in human brain by alternative splicing. However, the mouse genomic sequence did not conserve the 3' acceptor consensus sequence at the corresponding position, suggesting that type 2 neuropsin was a species-specific splice variant. When the open reading frames of **human neuropsin** were expressed in insect cells, both types of neuropsin

were detected in the conditioned media by western blot analysis using anti-**human neuropsin** serum. Northern blot hybridization and reverse transcription-polymerase chain reaction showed predominant expression of type 1 neuropsin in pancreas. Type 2 neuropsin was preferentially expressed in human adult brain and hippocampus, although both types were expressed in fetal brain and placenta in comparable amounts. Dot blot hybridization showed that neuropsin was expressed in various regions of adult brain, including the hippocampus and cerebral cortex, and also in various fetal tissues. These results suggest that human type 2 neuropsin may be important to the adult brain plasticity, although both types may be necessary for the development of the nervous system.

L3 ANSWER 16 OF 16 MEDLINE on STN DUPLICATE 3
1998372070. PubMed ID: 9714609. Sequence analysis and expression of **human neuropsin** cDNA and gene. Yoshida S; Taniguchi M; Hirata A; Shiosaka S. (Division of Structural Cell Biology, Nara Institute of Technology, 8916-5 Talayama Ikoma, Nara 630-1, Japan.) Gene, (1998 Jun 15) Vol. 213, No. 1-2, pp. 9-16. Journal code: 7706761. ISSN: 0378-1119. Pub. country: Netherlands. Language: English.

AB Neuropsin is a **serine protease** which is thought to function in a variety of tissues including the brain and skin. This protease has been shown to have important roles in neural plasticity in mice. Here we have cloned a cDNA and analyzed the gene for **human neuropsin** by polymerase chain reaction-based strategies. The cDNA had 72% identity to mouse neuropsin. The deduced amino acid sequence showed 72% identity to mouse neuropsin. Key amino acid residues for the enzyme activity and all cysteine residues were conserved between human and mouse neuropsin. The gene for **human neuropsin** had six exons and five introns, and the gene organization is similar to trypsin-type **serine proteases.** The mRNA was expressed in primary cultures of keratinocytes.

=> s l1 and TADG-14
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L5 18 DUP REMOVE L4 (5 DUPLICATES REMOVED)

=> d l5 1-18 cbib abs

L5 ANSWER 1 OF 18 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
2007:95583 Document No.: PREV200700092498. Extracellular **serine protease.** Anonymous; O'Brien, Timothy J. [Inventor]; Underwood, Lowell J. [Inventor]. Little Rock, AR USA. ASSIGNEE: The Board of Trustees of The University of Arkansas System. Patent Info.: US 07157084 20070102. Official Gazette of the United States Patent and Trademark Office Patents, (JAN 2 2007)
CODEN: OGUPE7. ISSN: 0098-1133. Language: English.

AB The present invention provides a DNA encoding a novel extracellular **serine protease** termed Tumor Antigen Derived Gene-14 (**TADG-14**) which is overexpressed in ovarian, breast and colon carcinoma samples. Also provided are vector and host cells capable of expressing the DNA of the present invention, as well as the uses of the DNA and protein of the present invention.

L5 ANSWER 2 OF 18 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 1
2006:649524 Document No.: PREV200600660908. Extracellular **serine protease.** Anonymous; Underwood, Lowell J. [Inventor]; O'Brien, Timothy J. [Inventor]. Little Rock, AR USA. ASSIGNEE: The University of Arkansas for Medical Sciences. Patent Info.: US 07067250 20060627.

Official Gazette of the United States Patent and Trademark Office Patents, (JUN 27 2006)
CODEN: OGUPE7. ISSN: 0098-1133. Language: English.

AB The present invention provides a DNA encoding a **TADG-14** protein selected from the group consisting of: (a) isolated DNA which encodes a **TADG-14** protein; (b) isolated DNA which hybridizes to isolated DNA of (a) above and which encodes a **TADG -14** protein; and (c) isolated DNA differing from the isolated DNAs of (a) and (b) above in codon sequence due to the degeneracy of the genetic code, and which encodes a **TADG-14** protein. Also provided is a vector capable of expressing the DNA of the present invention adapted for expression in a recombinant cell and regulatory elements necessary for expression of the DNA in the cell.

L5 ANSWER 3 OF 18 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
2007:605 Document No.: PREV200700006109. Extracellular **serine protease.** Anonymous; O'Brien, Timothy J. [Inventor]; Underwood, Lowell J. [Inventor]. Little Rock, AR USA. ASSIGNEE: The Board of Trustees of the University of Arkansas Systems. Patent Info.: US 07083790 20060801. Official Gazette of the United States Patent and Trademark Office Patents, (AUG 1 2006)
CODEN: OGUPE7. ISSN: 0098-1133. Language: English.

AB The present invention provides a DNA encoding a novel extracellular **serine protease** termed Tumor Antigen Derived Gene-14 (**TADG-14**) which is overexpressed in ovarian, breast and colon carcinoma samples. Also provided are vector and host cells capable of expressing the DNA of the present invention, as well as the uses of the DNA and protein of the present invention.

L5 ANSWER 4 OF 18 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
2006:356414 Document No.: PREV200600362355. Extracellular **serine protease.** O'Brien, Timothy J. [Inventor]; Underwood, Lowell J. [Inventor]. Little Rock, AR USA. ASSIGNEE: The Board of Trustees of the University of Arkansas. Patent Info.: US 07014993 20060321. Official Gazette of the United States Patent and Trademark Office Patents, (MAR 21 2006)
CODEN: OGUPE7. ISSN: 0098-1133. Language: English.

AB The present invention provides a DNA encoding a Tumor Antigen Derived Gene **TADG-14** protein selected from the group consisting of: (a) isolated DNA which encodes a **TADG-14** protein; (b) isolated DNA which hybridizes to isolated DNA of (a) above and which encodes a **TADG-14** protein; and (c) isolated DNA differing from the isolated DNAs of (a) and (b) above in codon sequence due to the degeneracy of the genetic code, and which encodes a **TADG-14** protein. Also provided is a vector capable of expressing the DNA of the present invention adapted for expression in a recombinant cell and regulatory elements necessary for expression of the DNA in the cell.

L5 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
2006:944746 Document No. 145:311201 Association between combinations of polymorphisms in the leptin gene and carcass traits in commercial feedlot steer and heifers. Woodward, Brent (Merial Limited, USA). PCT Int. Appl. WO 2006096427 A2 20060914, 106pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2006-US7326 20060302. PRIORITY: US 2005-658625P 20050304.

AB The invention provides a method for subgrouping animals according to genotype wherein the animals of each sub-group have a similar polymorphism

or combination of polymorphisms in the leptin gene, the single nucleotide polymorphisms being selected from the group consisting of UASMS1, UASMS2, UASMS3, EXON2-FB, and E2JW. The combination of single nucleotide polymorphisms of the leptin gene, especially combinations comprising alleles of the E2JW locus, may also indicate an increase in the tenderness of meat as well as indicating the quality of other traits of the animals. The invention also provides methods for identifying an animal having a desirable phenotype relating to certain feed intake, growth rate, body weight, carcass merit and composition, and milk yield, as compared to the general
population of animals of that species, comprising determining the presence of a single nucleotide polymorphism or combination of single nucleotide polymorphisms in the leptin gene of the animal.

L5 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
2006:952585 Document No. 145:309306 Cloning and sequence of the gene for human extracellular **serine protease TADG-14** and use in cancer diagnosis. O'Brien, Timothy J.; Underwood, Lowell J.; Beard, John; Shigemasa, Kazushi (USA). U.S. Pat. Appl. Publ. US 2006205054 A1 20060914, 52pp., Cont.-in-part of U.S. Ser. No. 796,294. (English). CODEN: USXXCO. APPLICATION: US 2003-652846 20030829. PRIORITY: US 1997-915659 19970821; US 1998-137944 19980821; US 2000-618259 20000718; US 2001-796294 20010228.
AB A cDNA for a novel extracellular **serine protease** termed Tumor Antigen Derived Gene-14 (**TADG-14** or neuropsin) is cloned and characterized. The gene for the enzyme is overexpressed in ovarian, breast and colon carcinoma samples. Also provided is a **TADG-14** protein splicing variant containing the sequence encoded by one of the genes introns that has a potential role for detecting and targeting of ovarian carcinomas. Epitopes of the enzymes that may be useful in tumor vaccines are identified.

L5 ANSWER 7 OF 18 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
2006:853761 The Genuine Article (R) Number: 078GL. Expression of tumor-associated differentially expressed gene-14 (**TADG-14**/KLK8) and its protein hK8 in uterine endometria and endometrial carcinomas. Jin H H; Nagai N (Reprint); Shigemasa K; Gu L J; Tanimoto H; Yunokawa M; Ohama K; Kudo Y; O'Brien T J. Hiroshima Univ, Grad Sch Biomed Sci, Dept Obstet & Gynecol, Minami Ku, 1-2-3 Kasumi, Hiroshima 7348551, Japan (Reprint); Hiroshima Univ, Grad Sch Biomed Sci, Dept Obstet & Gynecol, Minami Ku, Hiroshima 7348551, Japan; Fukuyama Med Ctr, Dept Obstet & Gynecol, Fukuyama, Hiroshima, Japan; Hiroshima City Asa Hosp, Dept Obstet & Gynecol, Hiroshima, Japan; Univ Tokyo, Inst Med Sci, Tokyo, Japan; Hiroshima Prefectural Hosp, Hiroshima, Japan; Univ Arkansas Med Sci, Dept Obstet & Gynecol, Little Rock, AR 72205 USA. n-nagai@asa-hosp.city.hiroshima.jp. TUMOR BIOLOGY (2006) Vol. 27, No. 5, pp. 274-282. ISSN: 1010-4283. Publisher: KARGER, ALLSCHWILERSTRASSE 10, CH-4009 BASEL, SWITZERLAND. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB To clarify the biological behavior of **TADG-14**/KLK8, we investigated **TADG-14**/KLK8 mRNA by semiquantitative RT-PCR and hK8 expression by immunohistochemistry using 37 normal endometria and 44 endometrial carcinoma tissues. **TADG-14**/KLK8 mRNA expression levels were significantly higher in proliferative compared to secretory phase endometria ($p = 0.0143$). Levels of TADG14/KLK8 mRNA expression correlated with hK8 protein levels. hK8 was detected in 73.3% (11/15) of endometria with a significantly higher detection rate in the proliferative compared to secretory and atrophic phase endometria ($p = 0.0002$). High expression of hK8 was found in 61.4% of endometrial carcinomas compared to 35.1% of endometrial tissue samples ($p = 0.0187$). hK8 expression was significantly higher in stage I ($p = 0.0433, 0.0038$) and grade 1/2 (G1/2) of the tumors ($p = 0.0195, 0.0044$). We suggest that expression of **TADG-14**/KLK8 may be regulated by sex steroid hormones in endometria. Our results indicate

that elevated **TADG-14**/KLK8 expression is an early event in endometrial carcinogenesis, and may potentially serve as a useful early biomarker for the detection of endometrial carcinomas in menopausal women. Copyright (c) 2006 S. Karger AG, Basel.

L5 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

2005:641679 Document No. 143:127832 Methods for the early diagnosis and targeted therapy of ovarian and other cancers by detecting and inhibiting PUMP-1 metalloprotease expression. O'Brien, Timothy J. (USA). U.S. Pat. Appl. Publ. US 2005158757 A1 20050721, 77 pp., Cont.-in-part of U.S. Ser. No. 172,597. (English). CODEN: USXXCO. APPLICATION: US 2004-12787 20041215. PRIORITY: US 1997-41404P 19970319; US 1998-39211 19980314; US 2000-492543 20000127; US 2001-835948 20010416; US 2002-172597 20020614.

AB This invention identifies PUMP-1 protease (matrix metalloprotease 7, matrilysin) as a marker for ovarian tumor cells, as well as a therapeutic intervention target. The genes which are clearly overexpressed include the **serine proteases** hepsin, stratum corneum chymotrypsin enzyme (SCCE), protease M, TADG12, TADG13, TADG14 and the metalloprotease PUMP-1. In various combinations with other proteases, PUMP-1 expression is characteristic of individual tumor types. The disclosed nucleic acid primer sets, used in combination with quant. amplification (PCR) of tissue cDNA, can indicate the presence of specific proteases in a tissue sample. The detected proteases are themselves specifically over-expressed in certain cancers, and their presence may serve for early detection of associated ovarian and other malignancies, and for the design of interactive therapies for cancer treatment. The invention provides methods of vaccinating an individual against PUMP-1 or produce immune-activated cells directed toward PUMP-1 by inoculating an individual with an expression vector encoding a PUMP-1 protein or a fragment thereof. The invention also provides methods of inhibiting expression of PUMP-1 in a cell by introducing into a cell a vector encoding an antisense PUMP-1 RNA or an antibody that binds the PUMP-1 protein.

L5 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

2004:927860 Document No. 142:293429 Neuropsin, human tissue kallikrein 8. Kishi, Tadaaki; Diamandis, Eleftherios P. (Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, ON, M5G 1X5, Can.). Handbook of Proteolytic Enzymes (2nd Edition), Volume 2, 1591-1593. Editor(s): Barrett, Alan J.; Rawlings, Neil D.; Woessner, J. Fred. Elsevier: London, UK. ISBN: 0-12-079610-4 (English) 2004. CODEN: 69GAQF.

AB A review. A novel **serine protease** that was predicted to have trypsin-like structure was cloned from a mouse hippocampus cDNA library and named neuropsin. Identified as a gene highly expressed in ovarian carcinoma, human neuropsin is also described as ovasin or tumor-associated differentially expressed gene 14 (**TADG-14**). Recently, the human neuropsin gene was mapped to chromosome 19q13.4 and identified as a member of the human kallikrein gene family. An international working party proposed to describe human neuropsin gene and protein as KLK8 and hK8, resp. The activity, specificity, structural chemical, preparation, biol. aspects, and distinguishing features of neuropsin or human kallikrein 8 are briefly discussed.

L5 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

2005:142430 Document No. 143:23849 Development of the new diagnostic and prognostic biomarker of ovarian cancer. Shigemasa, Kazushi (Department of Obstetrics and Gynecology, Graduate School of Biomedical Sciences, Hiroshima University, Hiroshima, Japan). Nippon Sanka Fujinka Gakkai Zasshi, 56(11), 1264-1274 (Japanese) 2004. CODEN: NISFAY. ISSN: 0300-9165. Publisher: Nippon Sanka Fujinka Gakkai.

AB To develop the new diagnostic and prognostic biomarker of ovarian cancer, we worked on the detection of new **serine proteases** as potential biomarker of ovarian cancer. We also worked on the mol. cloning of CA125 gene to develop the new CA125 assay system based on the CA125

gene structure. CA125 protein is composed of a short C-terminal domain, an extracellular superstructure dominated by repeat sequence, and a glycosylated N-terminal domain. Extracellular superstructure dominated by a repeat domain composed of 156 amino acid repeat units encompass the CA125 antibody (OC125 and M11) epitope binding sites. We developed the real-time PCR assay system targeting N-terminal domain to quantify CA125 mRNA expression and the assay system was compared to the similar assay system targeting the repeat units of CA125. Interestingly, the assay system targeting N-terminal domain showed the better sensitivity to detect early stage ovarian cancer compared to the assay system targeting CA125 repeat units. These results suggest that to develop new CA125 assay system using the new monoclonal antibody to determine CA125 N-terminal domain may be useful as a diagnostic tool for early stage ovarian cancer. To assess the value of secreted proteases as markers for early tumor detection and as targets for prognostic biomarker for ovarian cancer, we developed a strategy to detect **serine protease** genes differentially expressed in ovarian cancer using redundant primers to the amino acid sequences comprising the conserved catalytic triad domain of the **serine protease** family (viz. His-Asp-Ser). Using this approach, we have identified membrane type **serine proteases** including hepsin, TADG-12, TADG-15, and testisin. We also have identified secretory type **serine proteases** including protease M (KLK6), stratum corneum chymotryptic enzyme (SCCE/KLK7), and **TADG-14** (KLK8). These **serine proteases** are abundantly expressed in ovarian cancers compared to normal ovaries. Immunohistochem. showed that these **serine proteases** are expressed in ovarian cancer cells not in underlying stromal cells. The mRNA expression levels of these **serine proteases** including TADG-12, testisin, KLK5, and KLK7 are related with advanced clin. stage in ovarian cancer. The survival anal. showed that TADG-12, KLK5, KLK11, and KLK14 are related with poor prognosis in patients with ovarian cancer. These results suggest that the **serine proteases** identified here may play a role in development and progression of ovarian cancer and that some of these proteases may be useful as prognostic biomarker of ovarian cancer.

L5 ANSWER 11 OF 18 MEDLINE on STN DUPLICATE 2

2004048008. PubMed ID: 14749636. The novel **serine protease** tumor-associated differentially expressed gene-14 (KLK8/Neuropsin/Ovasin) is highly overexpressed in cervical cancer. Cane Stefania; Bignotti Eliana; Bellone Stefania; Palmieri Michela; De las Casas Luis; Roman Juan J; Pecorelli Sergio; Cannon Martin J; O'brien Timothy; Santin Alessandro D. (Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, University of Arkansas for Medical Sciences, Little Rock, AR 72205,USA.) American journal of obstetrics and gynecology, (2004 Jan) Vol. 190, No. 1, pp. 60-6. Journal code: 0370476. ISSN: 0002-9378. Pub. country: United States. Language: English.

AB OBJECTIVE: **Serine proteases** are redundant enzymes implicated in the extracellular modulation required for tumor growth and invasion. Tumor-associated differentially expressed gene-14 (**TADG -14**) is a novel transmembrane **serine protease** recently reported by our group to be highly overexpressed in ovarian carcinomas. The goal of this study was to investigate the frequency of expression of the **TADG-14** gene in human cervical tumors. STUDY DESIGN: **TADG-14** expression was evaluated in 19 cervical cancer cell lines (11 primary and 8 established cell lines) as well as in 8 normal cervical keratinocyte cultures by reverse transcriptase polymerase chain reaction. In addition, to validate gene expression data at the protein level, **TADG-14** expression was evaluated by immunohistochemistry on paraffin-embedded tissue from which all 11 primary tumor cell lines were established. RESULTS: **TADG-14** was found to be highly expressed in 82% (9/11) primary cervical cancer cell lines and in 87% (7/8) established cervical cancer cell lines by reverse transcriptase-polymerase chain

reaction. Expression of **TADG-14** by primary squamous cervical tumors was 100% (6/6), whereas 60% (3/5) of primary adenocarcinomas expressed **TADG-14**. In contrast, none of the normal cervical keratinocyte control cultures (n=4) or flash frozen normal cervical biopsy specimens (n=4) expressed **TADG-14** .. Immunohistochemistry staining of paraffin-embedded cervical cancer specimens confirmed **TADG-14** expression in tumor cells and its absence on normal cervical epithelial cells. CONCLUSION: Cervical cancer expressed a high level of **TADG-14**, suggesting that this protease may play an important role in invasion and metastasis. Because **TADG-14** appears only in abundance in tumor tissue and contains a secretion signal sequence, suggesting that **TADG-14** is secreted, it may prove to be a useful diagnostic tool for the early detection of recurrent/persistent cervical cancer after standard treatment or as a novel molecular target for cervical cancer therapy.

L5 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
2003:864031 Document No. 139:334830 Protein and cDNA sequences of a human extracellular **serine protease TADG-14** (tumor antigen derived gene-14). O'Brien, Timothy J.; Underwood, Lowell J. (The University of Arkansas for Medical Sciences, USA). U.S. US 6642013 B1 20031104, 44 pp., Cont.-in-part of U.S. Ser. No. 137,944. (English). CODEN: USXXAM. APPLICATION: US 2000-618259 20000718. PRIORITY: US 1997-915659 19970821; US 1998-137944 19980821.
AB The present invention provides a DNA encoding a novel extracellular **serine protease** termed tumor antigen derived gene-14 (**TADG-14**) which is overexpressed in ovarian, breast and colon carcinoma samples. Also provided are vector and host cells capable of expressing the DNA of the present invention, as well as the uses of the DNA and protein of the present invention.

L5 ANSWER 13 OF 18 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
2003:522239 Document No.: PREV200300522051. Transcription variants of the **serine protease** family may provide unique markers in cancer. O'Brien, T. J. [Reprint Author]; Beard, J. B. [Reprint Author]; Gu, L.; Sawasaki, T. [Reprint Author]; Shigemasa, K.. Department of Obstetrics and Gynecology, University of Arkansas for Medical Sciences, Little Rock, AR, USA. Tumor Biology, (August 2003) Vol. 24, No. Supplement 1, pp. 84. print.
Meeting Info.: XXXIst Meeting of the International Society for Oncodevelopmental Biology and Medicine. Edinburgh, UK. August 30-September 04, 2003. International Society for Oncodevelopmental Biology and Medicine.
ISSN: 1010-4283 (ISSN print). Language: English.

L5 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
2002:241295 Document No. 136:278129 Tumor antigen derived gene 14 (**TADG-14**) protein, polynucleotides and antibodies for diagnosis and therapy of cancer or carcinoma. O'Brien, Timothy J.; Underwood, Lowell J. (Uab Research Foundation, USA). U.S. Pat. Appl. Publ. US 2002037581 A1 20020328, 44 pp., Cont.-in-part of U. S. Ser. No. 618,259. (English). CODEN: USXXCO. APPLICATION: US 2001-796294 20010228. PRIORITY: US 1997-915659 19970821; US 1998-137944 19980821; US 2000-618259 20000718.
AB The present invention provides a DNA encoding a novel extracellular **serine protease** termed tumor antigen derived gene-14 (**TADG-14**) which is overexpressed in ovarian, breast and colon carcinoma samples. Also provided are vector and host cells capable of expressing the DNA of the present invention, as well as antibodies or fragment to **TADG-14** protein, antisense DNA, oligonucleotide probes, etc. for use in diagnosis and treatment of cancer or carcinoma, and in drug screening.

L5 ANSWER 15 OF 18 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

2002220949 EMBASE Novel immunotherapeutic strategies in gynecologic oncology: Dendritic cell-based immunotherapy for ovarian cancer. Santin A.D.; Bellone S.; Underwood L.J.; O'Brien T.J.; Ravaggi A.; Pecorelli S.; Cannon M.J.. A.D. Santin, Univ. of Arkansas for Med. Sciences, 4301 West Markham, Little Rock, AR 72205, United States. santinalessandrod@uams.edu. Minerva Ginecologica Vol. 54, No. 2, pp. 133-144 2002.
Refs: 80.
ISSN: 0026-4784. CODEN: MIGIA6
Pub. Country: Italy. Language: English. Summary Language: English; Italian.
Entered STN: 20020711. Last Updated on STN: 20020711

AB The recognition of tumor antigen loaded dendritic cells as one of the most promising approaches to induce a tumor specific immune response in vivo has recently generated widespread interest in the use of these "natural adjuvants" for the therapy of human malignancies refractory to standard treatment modalities. However, many cancer patients may not benefit from current strategies of cancer vaccination because an effective tumor antigen associated with their cancer has not yet been identified or because sufficient amounts of tumor tissue cannot be obtained for antigen preparation. The recent identification and cloning of a group of preferentially expressed **serine proteases** as novel ovarian tumor-associated antigens may offer the opportunity to test in a large group of patients the potential of DC-based immunotherapy. In this review, we describe these ovarian tumor antigens and assess the potential for therapeutic DC vaccination for the treatment of chemotherapy-resistant ovarian cancer.

L5 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

2001:830873 Document No. 135:368950 Screening for PUMP-1, SCCE and hepsin proteases for diagnosis of ovarian, breast and lung cancer. O'brien, Timothy J. (The Board of Trustees of the University of Arkansas, USA). U.S. US 6316213 B1 20011113, 70 pp., Cont.-in-part of U.S. Ser. No. 39,211. (English). CODEN: USXXAM. APPLICATION: US 2000-492543 20000127. PRIORITY: US 1997-PV41404 19970319; US 1998-39211 19980313.

AB A method for diagnosing ovarian, breast or lung cancer comprising detection of PUMP-1 protease in body fluids or tumors by immunoassay, hybridization and flow cytometry is disclosed. Detection of hepsin and SCCE as well as PUMP-1 in biol. samples may be used for detection of malignant, ovarian, lung or breast hyperplasia. Redundant primers to conserved domains of serine, metallo- and cysteine proteases have yielded a set of genes whose mRNAs are overexpressed in ovarian carcinoma. These genes encode hepsin, SCCE, protease M, TADG12, TADG14 and PUMP-1 (matrix metalloprotease 7). Northern blots of normal and ovarian carcinoma tissues indicated overexpression of hepsin, SCCE, PUMP-1 and **TADG -14.**

L5 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

1999:549168 Document No. 131:181664 TADG-15: an extracellular **serine protease** overexpressed in breast and ovarian carcinomas. O'Brien, Timothy J.; Tanimoto, Hirotoshi (The Board of Trustees of the University of Arkansas, USA). PCT Int. Appl. WO 9942120 A1 19990826, 71 pp. DESIGNATED STATES: W: AU, CA, JP; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US3436 19990218. PRIORITY: US 1998-27337 19980220.

AB The invention provides a cDNA encoding a novel human extracellular **serine protease** termed Tumor Antigen Derived Gene-15 (TADG-15). The cDNA sequence as well as the corresponding deduced amino acid sequence of human TADG-15 are disclosed. Also disclosed is a vector capable of expressing the human TADG-15 when transfected into a foreign host cell. In addition, a method (nucleic acid hybridization) for detecting the level of **TADG-14** gene mRNA is disclosed. The TADG-15 **serine protease** has been found to be overexpressed in breast and ovarian carcinomas. PCR primers specific for

the TADG-15 gene were constructed and used to show expression of TADG-15 mRNA in ovarian carcinomas. Due to the extracellular nature of the TADG-15 **serine protease**, it may be possible to exploit its expression as a diagnostic tool for ovarian cancer.

L5 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
1999:139935 Document No. 130:206695 Novel extracellular **serine protease.** O'Brien, Timothy J.; Underwood, Lowell J. (Board of Trustees of the University of Arkansas, USA). PCT Int. Appl. WO 9909138 A1 19990225, 62 pp. DESIGNATED STATES: W: AU, CA, JP; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US17372 19980821. PRIORITY: US 1997-915659 19970821.
AB The invention provides a cDNA encoding a novel human extracellular **serine protease** termed tumor antigen derived gene 14 (**TADG-14**). The cDNA sequence, as well as the corresponding deduced amino acid sequence of human **TADG-14** are disclosed. Also disclosed is a vector capable of expressing the human **TADG-14** when transfected into a foreign host cell. In addition, a method (nucleic acid hybridization) for detecting the level of **TADG-14** gene mRNA is disclosed. Comparison of the deduced **TADG-14** amino acid sequence with sequences of known proteases revealed significant similarity with human glandular kallikrein, PSA and protease M, and mouse neuropsin. The human **TADG-14** showed the most homol. to mouse neuropsin, and it may represent the human equivalent or may be a member of neuropsin-like **serine proteases**. The TADG-**14 serine protease** was found in to be expressed in ovarian, breast and colon carcinomas. PCR primers specific for the **TADG-14** gene were constructed and used to show expression of **TADG-14** mRNA in ovarian carcinomas. Due to the extracellular nature of the **TADG-14 serine protease**, it may be possible to exploit its expression as a diagnostic tool for ovarian cancer.

=> s (Obrien t?/au or underwood l?/au or beard j?/au or shigemasa k?/au)
L6 6353 (OBRIEN T?/AU OR UNDERWOOD L?/AU OR BEARD J?/AU OR SHIGEMASA K?/AU)

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L7 84 L6 AND SERINE PROTEASE

=> s l7 and TADG-14
L8 13 L7 AND TADG-14

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L9 12 DUP REMOVE L8 (1 DUPLICATE REMOVED)

=> d l9 1-12 cbib abs

L9 ANSWER 1 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
2007:95583 Document No.: PREV200700092498. Extracellular **serine protease.** Anonymous; O'Brien, Timothy J. [Inventor]; **Underwood, Lowell J.** [Inventor]. Little Rock, AR USA. ASSIGNEE: The Board of Trustees of The University of Arkansas System. Patent Info.: US 07157084 20070102. Official Gazette of the United States Patent and Trademark Office Patents, (JAN 2 2007)
CODEN: OGUPE7. ISSN: 0098-1133. Language: English.
AB The present invention provides a DNA encoding a novel extracellular **serine protease** termed Tumor Antigen Derived Gene-14 (**TADG-14**) which is overexpressed in ovarian, breast and colon carcinoma samples. Also provided are vector and host cells capable of expressing the DNA of the present invention, as well as the uses of the

DNA and protein of the present invention.

L9 ANSWER 2 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 1
2006:649524 Document No.: PREV200600660908. Extracellular **serine protease.** Anonymous; **Underwood, Lowell J.** [Inventor]; O'Brien, Timothy J. [Inventor]. Little Rock, AR USA. ASSIGNEE: The University of Arkansas for Medical Sciences. Patent Info.: US 07067250 20060627. Official Gazette of the United States Patent and Trademark Office Patents, (JUN 27 2006)
CODEN: OGUPE7. ISSN: 0098-1133. Language: English.
AB The present invention provides a DNA encoding a **TADG-14** protein selected from the group consisting of: (a) isolated DNA which encodes a **TADG-14** protein; (b) isolated DNA which hybridizes to isolated DNA of (a) above and which encodes a **TADG -14** protein; and (c) isolated DNA differing from the isolated DNAs of (a) and (b) above in codon sequence due to the degeneracy of the genetic code, and which encodes a **TADG-14** protein. Also provided is a vector capable of expressing the DNA of the present invention adapted for expression in a recombinant cell and regulatory elements necessary for expression of the DNA in the cell.

L9 ANSWER 3 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
2007:605 Document No.: PREV200700006109. Extracellular **serine protease.** Anonymous; O'Brien, Timothy J. [Inventor]; **Underwood, Lowell J.** [Inventor]. Little Rock, AR USA. ASSIGNEE: The Board of Trustees of the University of Arkansas Systems. Patent Info.: US 07083790 20060801. Official Gazette of the United States Patent and Trademark Office Patents, (AUG 1 2006)
CODEN: OGUPE7. ISSN: 0098-1133. Language: English.
AB The present invention provides a DNA encoding a novel extracellular **serine protease** termed Tumor Antigen Derived Gene-14 (**TADG-14**) which is overexpressed in ovarian, breast and colon carcinoma samples. Also provided are vector and host cells capable of expressing the DNA of the present invention, as well as the uses of the DNA and protein of the present invention.

L9 ANSWER 4 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
2006:356414 Document No.: PREV200600362355. Extracellular **serine protease.** O'Brien, Timothy J. [Inventor]; **Underwood, Lowell J.** [Inventor]. Little Rock, AR USA. ASSIGNEE: The Board of Trustees of the University of Arkansas. Patent Info.: US 07014993 20060321. Official Gazette of the United States Patent and Trademark Office Patents, (MAR 21 2006)
CODEN: OGUPE7. ISSN: 0098-1133. Language: English.
AB The present invention provides a DNA encoding a Tumor Antigen Derived Gene **TADG-14** protein selected from the group consisting of: (a) isolated DNA which encodes a **TADG-14** protein; (b) isolated DNA which hybridizes to isolated DNA of (a) above and which encodes a **TADG-14** protein; and (c) isolated DNA differing from the isolated DNAs of (a) and (b) above in codon sequence due to the degeneracy of the genetic code, and which encodes a **TADG-14** protein. Also provided is a vector capable of expressing the DNA of the present invention adapted for expression in a recombinant cell and regulatory elements necessary for expression of the DNA in the cell.

L9 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
2006:952585 Document No. 145:309306 Cloning and sequence of the gene for human extracellular **serine protease TADG-14** and use in cancer diagnosis. O'Brien, Timothy J.; **Underwood, Lowell J.**; **Beard, John**; **Shigemasa, Kazushi** (USA). U.S. Pat. Appl. Publ. US 2006205054 A1 20060914, 52pp., Cont.-in-part of U.S. Ser. No. 796,294. (English). CODEN: USXXCO. APPLICATION: US 2003-652846 20030829. PRIORITY: US 1997-915659 19970821;

US 1998-137944 19980821; US 2000-618259 20000718; US 2001-796294 20010228.

AB A cDNA for a novel extracellular **serine protease** termed Tumor Antigen Derived Gene-14 (**TADG-14** or neuropsin) is cloned and characterized. The gene for the enzyme is overexpressed in ovarian, breast and colon carcinoma samples. Also provided is a **TADG-14** protein splicing variant containing the sequence encoded by one of the genes introns that has a potential role for detecting and targeting of ovarian carcinomas. Epitopes of the enzymes that may be useful in tumor vaccines are identified.

L9 ANSWER 6 OF 12 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

2006:853761 The Genuine Article (R) Number: 078GL. Expression of tumor-associated differentially expressed gene-14 (**TADG-14**/KLK8) and its protein hK8 in uterine endometria and endometrial carcinomas. Jin H H; Nagai N (Reprint); **Shigemasa K**; Gu L J; Tanimoto H; Yunokawa M; Ohama K; Kudo Y; O'Brien T J. Hiroshima Univ, Grad Sch Biomed Sci, Dept Obstet & Gynecol, Minami Ku, 1-2-3 Kasumi, Hiroshima 7348551, Japan (Reprint); Hiroshima Univ, Grad Sch Biomed Sci, Dept Obstet & Gynecol, Minami Ku, Hiroshima 7348551, Japan; Fukuyama Med Ctr, Dept Obstet & Gynecol, Fukuyama, Hiroshima, Japan; Hiroshima City Asa Hosp, Dept Obstet & Gynecol, Hiroshima, Japan; Univ Tokyo, Inst Med Sci, Tokyo, Japan; Hiroshima Prefectural Hosp, Hiroshima, Japan; Univ Arkansas Med Sci, Dept Obstet & Gynecol, Little Rock, AR 72205 USA. n-nagai@asa-hosp.city.hiroshima.jp. TUMOR BIOLOGY (2006) Vol. 27, No. 5, pp. 274-282. ISSN: 1010-4283. Publisher: KARGER, ALLSCHWILERSTRASSE 10, CH-4009 BASEL, SWITZERLAND. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB To clarify the biological behavior of **TADG-14**/KLK8, we investigated **TADG-14**/KLK8 mRNA by semiquantitative RT-PCR and hK8 expression by immunohistochemistry using 37 normal endometria and 44 endometrial carcinoma tissues. **TADG-14**/KLK8 mRNA expression levels were significantly higher in proliferative compared to secretory phase endometria ($p = 0.0143$). Levels of TADG14/KLK8 mRNA expression correlated with hK8 protein levels. hK8 was detected in 73.3% (11/15) of endometria with a significantly higher detection rate in the proliferative compared to secretory and atrophic phase endometria ($p = 0.0002$). High expression of hK8 was found in 61.4% of endometrial carcinomas compared to 35.1% of endometrial tissue samples ($p = 0.0187$). hK8 expression was significantly higher in stage I ($p = 0.0433, 0.0038$) and grade 1/2 (G1/2) of the tumors ($p = 0.0195, 0.0044$). We suggest that expression of **TADG-14**/KLK8 may be regulated by sex steroid hormones in endometria. Our results indicate that elevated **TADG-14**/KLK8 expression is an early event in endometrial carcinogenesis, and may potentially serve as a useful early biomarker for the detection of endometrial carcinomas in menopausal women. Copyright (c) 2006 S. Karger AG, Basel.

L9 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

2005:142430 Document No. 143:23849 Development of the new diagnostic and prognostic biomarker of ovarian cancer. **Shigemasa, Kazushi** (Department of Obstetrics and Gynecology, Graduate School of Biomedical Sciences, Hiroshima University, Hiroshima, Japan). Nippon Sanka Fujinka Gakkai Zasshi, 56(11), 1264-1274 (Japanese) 2004. CODEN: NISFAY. ISSN: 0300-9165. Publisher: Nippon Sanka Fujinka Gakkai.

AB To develop the new diagnostic and prognostic biomarker of ovarian cancer, we worked on the detection of new **serine proteases** as potential biomarker of ovarian cancer. We also worked on the mol. cloning of CA125 gene to develop the new CA125 assay system based on the CA125 gene structure. CA125 protein is composed of a short C-terminal domain, an extracellular superstructure dominated by repeat sequence, and a glycosylated N-terminal domain. Extracellular superstructure dominated by a repeat domain composed of 156 amino acid repeat units encompass the CA125 antibody (OC125 and M11) epitope binding sites. We developed the real-time PCR assay system targeting N-terminal domain to quantify CA125

mRNA expression and the assay system was compared to the similar assay system targeting the repeat units of CA125. Interestingly, the assay system targeting N-terminal domain showed the better sensitivity to detect early stage ovarian cancer compared to the assay system targeting CA125 repeat units. These results suggest that to develop new CA125 assay system using the new monoclonal antibody to determine CA125 N-terminal domain may be useful as a diagnostic tool for early stage ovarian cancer. To assess the value of secreted proteases as markers for early tumor detection and as targets for prognostic biomarker for ovarian cancer, we developed a strategy to detect **serine protease** genes differentially expressed in ovarian cancer using redundant primers to the amino acid sequences comprising the conserved catalytic triad domain of the **serine protease** family (viz. His-Asp-Ser). Using this approach, we have identified membrane type **serine proteases** including hepsin, TADG-12, TADG-15, and testisin. We also have identified secretory type **serine proteases** including protease M (KLK6), stratum corneum chymotryptic enzyme (SCCE/KLK7), and TADG-14 (KLK8). These **serine proteases** are abundantly expressed in ovarian cancers compared to normal ovaries. Immunohistochem. showed that these **serine proteases** are expressed in ovarian cancer cells not in underlying stromal cells. The mRNA expression levels of these **serine proteases** including TADG-12, testisin, KLK5, and KLK7 are related with advanced clin. stage in ovarian cancer. The survival anal. showed that TADG-12, KLK5, KLK11, and KLK14 are related with poor prognosis in patients with ovarian cancer. These results suggest that the **serine proteases** identified here may play a role in development and progression of ovarian cancer and that some of these proteases may be useful as prognostic biomarker of ovarian cancer.

L9 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
2003:864031 Document No. 139:334830 Protein and cDNA sequences of a human extracellular **serine protease TADG-14** (tumor antigen derived gene-14). O'Brien, Timothy J.; **Underwood, Lowell J.** (The University of Arkansas for Medical Sciences, USA). U.S. US 6642013 B1 20031104, 44 pp., Cont.-in-part of U.S. Ser. No. 137,944. (English). CODEN: USXXAM. APPLICATION: US 2000-618259 20000718. PRIORITY: US 1997-915659 19970821; US 1998-137944 19980821.

AB The present invention provides a DNA encoding a novel extracellular **serine protease** termed tumor antigen derived gene-14 (**TADG-14**) which is overexpressed in ovarian, breast and colon carcinoma samples. Also provided are vector and host cells capable of expressing the DNA of the present invention, as well as the uses of the DNA and protein of the present invention.

L9 ANSWER 9 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
2003:522239 Document No.: PREV200300522051. Transcription variants of the **serine protease** family may provide unique markers in cancer. O'Brien, T. J. [Reprint Author]; **Beard, J. B.** [Reprint Author]; Gu, L.; Sawasaki, T. [Reprint Author]; **Shigemasa, K.**. Department of Obstetrics and Gynecology, University of Arkansas for Medical Sciences, Little Rock, AR, USA. Tumor Biology, (August 2003) Vol. 24, No. Supplement 1, pp. 84. print.
Meeting Info.: XXXIst Meeting of the International Society for Oncodevelopmental Biology and Medicine. Edinburgh, UK. August 30-September 04, 2003. International Society for Oncodevelopmental Biology and Medicine.
ISSN: 1010-4283 (ISSN print). Language: English.

L9 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
2002:241295 Document No. 136:278129 Tumor antigen derived gene 14 (**TADG-14**) protein, polynucleotides and antibodies for diagnosis and therapy of cancer or carcinoma. O'Brien, Timothy J.; **Underwood, Lowell J.** (Uab Research Foundation, USA). U.S. Pat.

Appl. Publ. US 2002037581 A1 20020328, 44 pp., Cont.-in-part of U. S. Ser. No. 618,259. (English). CODEN: USXXCO. APPLICATION: US 2001-796294 20010228. PRIORITY: US 1997-915659 19970821; US 1998-137944 19980821; US 2000-618259 20000718.

AB The present invention provides a DNA encoding a novel extracellular **serine protease** termed tumor antigen derived gene-14 (**TADG-14**) which is overexpressed in ovarian, breast and colon carcinoma samples. Also provided are vector and host cells capable of expressing the DNA of the present invention, as well as antibodies or fragment to **TADG-14** protein, antisense DNA, oligonucleotide probes, etc. for use in diagnosis and treatment of cancer or carcinoma, and in drug screening.

L9 ANSWER 11 OF 12 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

2002220949 EMBASE Novel immunotherapeutic strategies in gynecologic oncology: Dendritic cell-based immunotherapy for ovarian cancer. Santin A.D.; Bellone S.; **Underwood L.J.**; O'Brien T.J.; Ravaggi A.; Pecorelli S.; Cannon M.J.. A.D. Santin, Univ. of Arkansas for Med. Sciences, 4301 West Markham, Little Rock, AR 72205, United States. santinalessandrod@uams.edu. Minerva Ginecologica Vol. 54, No. 2, pp. 133-144 2002.
Refs: 80.
ISSN: 0026-4784. CODEN: MIGIA6
Pub. Country: Italy. Language: English. Summary Language: English; Italian.
Entered STN: 20020711. Last Updated on STN: 20020711

AB The recognition of tumor antigen loaded dendritic cells as one of the most promising approaches to induce a tumor specific immune response in vivo has recently generated widespread interest in the use of these "natural adjuvants" for the therapy of human malignancies refractory to standard treatment modalities. However, many cancer patients may not benefit from current strategies of cancer vaccination because an effective tumor antigen associated with their cancer has not yet been identified or because sufficient amounts of tumor tissue cannot be obtained for antigen preparation. The recent identification and cloning of a group of preferentially expressed **serine proteases** as novel ovarian tumor-associated antigens may offer the opportunity to test in a large group of patients the potential of DC-based immunotherapy. In this review, we describe these ovarian tumor antigens and assess the potential for therapeutic DC vaccination for the treatment of chemotherapy-resistant ovarian cancer.

L9 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

1999:139935 Document No. 130:206695 Novel extracellular **serine protease.** O'Brien, Timothy J.; **Underwood, Lowell J.** (Board of Trustees of the University of Arkansas, USA). PCT Int. Appl. WO 9909138 A1 19990225, 62 pp. DESIGNATED STATES: W: AU, CA, JP; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US17372 19980821. PRIORITY: US 1997-915659 19970821.

AB The invention provides a cDNA encoding a novel human extracellular **serine protease** termed tumor antigen derived gene 14 (**TADG-14**). The cDNA sequence, as well as the corresponding deduced amino acid sequence of human **TADG-14** are disclosed. Also disclosed is a vector capable of expressing the human **TADG-14** when transfected into a foreign host cell. In addition, a method (nucleic acid hybridization) for detecting the level of **TADG-14** gene mRNA is disclosed. Comparison of the deduced **TADG-14** amino acid sequence with sequences of known proteases revealed significant similarity with human glandular kallikrein, PSA and protease M, and mouse neuropsin. The human **TADG-14** showed the most homol. to mouse neuropsin, and it may represent the human equivalent or may be a member of neuropsin-like **serine proteases.** The **TADG-**

14 serine protease was found in to be expressed in ovarian, breast and colon carcinomas. PCR primers specific for the **TADG-14** gene were constructed and used to show expression of **TADG-14** mRNA in ovarian carcinomas. Due to the extracellular nature of the **TADG-14** **serine protease**, it may be possible to exploit its expression as a diagnostic tool for ovarian cancer.

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	178.39	178.60

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
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